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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,203	12/06/2000	Markus Kalkum	1539-00	7336

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EXAMINER	
GORDON, BRIAN R	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 10/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/701,203	KALKUM ET AL.
	Examiner	Art Unit
	Brian R. Gordon	1743

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8-25-04* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,23-30 and 32-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *20 and 23-29* is/are allowed.

6)☒ Claim(s) *30 and 32-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 December 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. PCT/EP99/03667, filed on May 27, 1999.

Response to Arguments

2. Applicant's arguments filed August 25, 2004 have been fully considered but they are not persuasive. Applicant asserts the subject of Claim 30 is novel over Tajima.

As to Tajima and the inherency of the device being classified as a microdosing device, "the Applicants respectfully submit that no such inherency in Tajima is disclosed, either explicitly or implicitly. There is utterly no relationship between the capability of manipulating microorganisms on the one hand and the size of the device used for such manipulation on the other hand."

The examiner respectfully disagrees, for Tajima column 4, first paragraph discloses "the present invention is well suited to works of separating, taking out, pipetting, clarifying, condensing, diluting and/or works of capturing, extracting, isolating, amplifying, labeling, and measuring molecule level organisms or **microorganisms** such as cells, DNA, RNA, mRNA, plasmid, virus, and bacteria or certain high molecular substance, and a target high molecular substance can be obtained without depending on the conventional centrifugation." As disclosed above the device is useful with micro scale particles as such it may be inherently classified as a mirodoser, micropipette, or

microdispenser. All of the body fluids and other high molecular substances mentioned are conventionally known in the art to be sampled or analyzed in microdoses.

As to the relationship of the microorganisms and size of the device, this is an issue that is not commensurate in scope with that of claim 30. The claim makes no reference to the size of the device.

Applicant further states, "According to Tajima, operation of the magnets does not allow a predetermined motion of the magnetic particles in the microdosing device with the magnetic forces of the magnets. If the particles are released from the magnets, they would move under the influence of gravity, but not under the influence of magnetic forces."

The argument is not commensurate in scope with that of the claim. The claim does not require "predetermined motion" of the magnetic particles. Furthermore, there is nothing in the claim directed to what happens when the magnetic force is release. The argument is not based on any structural differences between the instant invention and the applied prior art. Even if such an issue was present, gravity results in a predetermined movement of the particles in a downward direction.

The argument is directed to an intended use clause of the claim.

It has been held that a recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus satisfying the claimed structural limitations. Ex parte Masham, 2 USPQ2d 1647 (1987).

It has been held that the recitation that an element is "adapted to" perform or is "capable of" performing a function is not a positive limitation but only requires the ability to so perform.

The examiner asserts that activation of the magnet causes the magnetic particles in the fluid to all move in a predetermined aimed direction (toward the magnet location).

As to the 103 rejection, applicant asserts Figure 2 of the device of Tajima suggests the device is adapted for handling ml volumes rather than μl or nl volumes. After reviewing the text and Figure 2, there is no such suggestion stated or illustrated for there is no volumetric measurement or scale shown in the figures. Furthermore, the dimensions of the device are not mention nor given in the Figure for applicant to derive at such a conclusion based on the Figures submitted by Tajima. However, the dimensions of a dispensing device are not reflective of the ability of the device to dispense minute volumes. There is no direct correlation of size of the device and ability to dispense stated within the prior art.

Applicant further provides remarks directed to the differences in utilization in that of the device of Tajima and that of the instant application. As previously recited intended use is not an issue of patentability. The differences must be shown in terms of structure.

For reasons given herein above and below the 102 rejection of claims 30 and 32-36 and the 103 rejection of claims 37-38 are hereby maintained.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claims 30 and 32-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Tajima US 5,895,631.

Tajima teaches a method making use of a pipette device which sucks a liquid containing a target high molecular substance via a chip detachably set in a sucking port or a discharging port of a liquid sucking/discharging line from inside of a vessel and transfers the liquid or the target high molecular substance to a target next processing position, and the chip has the sucked target high molecular substance deposited on magnetic particles (solid carrier material) and/or separated with a filter set in the chip. Namely, it is possible to automatically execute with high precision the works of quantifying, separating, taking out, pipetting, clarifying, condensing, diluting a liquid or a target high molecular substance as well as works of extracting, recovering, and isolating the substance by controlling the pipette device's operations for sucking and discharging the liquid and magnetic particles with a magnetic body and/or by a combination of a magnetic body and a filter (pourous carrier material).

The target high molecular substance is a useful substance such as antibiotics, genetic substances such ad DNA, or an immunological substance such as antibody. For this reason, the present invention is well suited to works of separating, taking out, pipetting, clarifying, condensing, diluting and/or works of capturing, extracting, isolating, amplifying, labelling, and measuring molecule level organisms or microorganisms such as cells, DNA, RNA, mRNA, plasmid, virus, and bacteria or certain high molecular substance, and a target high molecular substance can be obtained without depending on the conventional centrifugation.

By having a target high molecular substance or a substance bonded to a target high molecular substance absorbed or bonded to a surface of each magnetic particle used for the purpose of the present invention, the target high molecular substance can be obtained without executing centrifugation.

In the present invention, in a case where the above-described magnetic particles are used, controls are provided so that the magnetic particles are absorbed onto an internal wall of a chip due to a magnetic force working from outside of the chip, or so that, if effect of the magnetic force is weak or not present, the magnetic particles are held separable from the internal surface of the chip, it is possible to control capture of target high molecular substance and separation of the same from foreign materials with high precision.

There is provided a liquid processing apparatus making use of a pipette device (microdosing device) comprising a liquid sucking/discharging line which can move in the horizontal line and is maintained at a specified position so that it can move in the

vertical direction, a plurality of chips required for processing one type of liquid and provided along the horizontal line in which this sucking/discharging line moves, a vessel with the liquid accommodated therein, one or more filter holders each having a filter set therein required for the processing described above, one or more vessels each accommodating therein other types of liquid required for the processing above, a vessel in which a liquid containing magnetic particles is accommodated, and a magnetic body for attracting the magnetic particles onto an internal surface of the chip in the process of sucking or discharging a solution containing the magnetic particles, and the liquid sucking/discharging line is transferred according to instructions from a control unit to execute required processing for a liquid or a target high molecular substance contained in the liquid, and for this reason it is possible to execute such works as quantifying, separating, taking out, pipetting, clarifying, condensing, diluting a target high molecular substance and also such complicated works as extracting, recovering, and isolating the target high molecular substance with very simple configuration in succession and automatically.

In a case where the magnetic body is built with a permanent magnet, a surface of the **permanent magnet** (drive device) contacting a chip is formed according to an external form of the chip and the chip is movably provided in a direction perpendicular to the longitudinal direction of the chip, so that it is possible not only to completely capture magnetic particles, but also to prevent adverse effects by diffusion and movement of the magnetic particles in association with the magnet without fail.

The magnetic body may also be built with an **electric magnet** (drive device) in place of the permanent magnet described above with a surface thereof contacting a chip formed according to an external form of the chip, and is provided so that the electric magnet generates a magnetic force when it contacts outside of the chip and also can move, when degaussed, in a direction perpendicular to the longitudinal center line of the chip or in a range including the direction, and for this reason magnetic particles are attracted in association with movement of the magnetic body along the longitudinal center line of the chip so that it is possible to prevent the magnetic particles from going out of control and control over the magnetic particles from being lost, which makes it possible to realize complete attraction of the magnetic particles.

Tajima also teaches a step of subjecting DNA refined through the reaction steps as given in relation to such works as extracting, recovering, isolating or amplifying with PCR or to control for temperature thereof.

Namely, in a case where such works as extracting, recovering, or isolating by making use of this pipette device with magnetic particles G with DNA or DNA-bonded substance bonded to the surface, as shown in step 14 in FIG. 13, at first the pipette nozzle P is moved upward and then transferred to just above a fourth cell C_4 with the second filter holder H_2 left in cell C_3 via a filter holder removing body E_2 having the same configuration as that of the filter holder removing body E_1 and the sucked DNA solution is discharged into the cell C_4.

A required quantity of reaction liquid containing magnetic particles G with DNA or DNA-bonded substance bonded to the surface thereof has been supplied into this cell C_4, and when the DNA solution is discharged into the reaction liquid, a reaction between DNA fragments and the magnetic particles G is started.

The chip T_3 with the DNA solution having been discharged into the cell C_4 is removed from the lower edge section of the pipette nozzle P according to the processing sequence like in a case of the chip T_1 or chip T_2, and is aborted.

It is needless to say that then the chip T_4 is set in the lower edge section of the pipette nozzle P according to the processing sequence as described above.

Then, after a certain period of time has passed, the pipette nozzle P goes downward and steeps the chip T_4 into the reaction liquid, the magnetic body M contacts the intermediate diameter section K_{12} of the chip T_4, the works of sucking and discharging the liquid by the pipette nozzle P is executed at least once according to the necessity, and separation between the magnetic particles and the reaction liquid is executed (step 15). Then the sucking and discharging work is executed to a slow speed so that almost all the magnetic particles are captured. In this case, it is important for completely attracting the magnetic particles to provide controls over the sucking and discharging operations so that the final liquid surface of the reaction liquid sucked or discharged passes through an area effected by a magnetic force generated by the magnetic body M.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tajima as applied to claims 30 and 32-36 above, and further in view of Papen et al. US 6,083,762.

Tajima does not teach that the device comprises piezoelectric pipettes with a volume of less than 500 microliters.

Papen et al. discloses a low volume liquid handling system is which includes a microdispenser employing a piezoelectric transducer attached to a glass capillary, a positive displacement pump for priming and aspirating liquid into the microdispenser, controlling the pressure of the liquid system, and washing the microdispenser between liquid transfers, and a pressure sensor to measure the liquid system pressure and produce a corresponding electrical signal.

The microdispenser is capable of rapidly and accurately dispensing sub-nanoliter ("nl") sized droplets by forcibly ejecting the droplets from a small nozzle.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the device of Tajima by employing a piezoelectric transducer as taught by Papen to provide a microvolume liquid handling system which can transfer microvolume quantities of fluids containing chemically or biologically active substances. The piezoelectric transducer allows for accurate dispensing of sub-nanoliter size individual droplets which are very reproducible.

Allowable Subject Matter

9. Claims 20 and 23-29 are allowed.

10. The following is a statement of reasons for the indication of allowable subject matter: The prior art of record does not teach nor fairly suggest a method for processing at least one substance in a reservoir of a microdosing device, said

microdosing device being a micropipette or a microdispenser and said reservoir having an outlet being adapted for microdroplet delivery comprising the steps of:

arranging a solid carrier material as a solid phase with a binding-active surface in the reservoir, said carrier material being held with a drive device located outside said reservoir; collecting the substance in the reservoir by repeatedly performing the steps of uptaking a solution or suspension liquid with the substance into the reservoir, repeatedly moving the carrier material in the reservoir with said drive device and binding the substance to a surface of the carrier material and delivering the remaining liquid from the reservoir; and uptaking an elution agent separating the bound substance from the carrier material or a reaction partner reacting with the substance in the reservoir.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Gordon whose telephone number is 571-272-1258. The examiner can normally be reached on M-F, with 2nd and 4th F off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

brg

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